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Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction

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ABSTRACT

BACKGROUND Despite advances in treatment, mortality in acute myocardial infarction (AMI) complicated by cardiogenic shock (CS) remains high. Short-term mechanical circulatory support devices acutely improve hemodynamic conditions.

OBJECTIVES The aim of this study was to determine whether a new percutaneous mechanical circulatory support (pMCS) device (Impella CP, Abiomed, Danvers, Massachusetts) decreases 30-day mortality when compared with an intra-aortic balloon pump (IABP) in patients with severe shock complicating AMI.

METHODS In a randomized, prospective, open-label, multicenter trial, 48 patients with severe CS complicating AMI were assigned to pMCS (n = 24) or IABP (n = 24). Severe CS was defined as systolic blood pressure <90 mm Hg or the need for inotropic or vasoactive medication and the requirement for mechanical ventilation. The primary endpoint was 30-day all-cause mortality.

RESULTS At 30 days, mortality in patients treated with either IABP or pMCS was similar (50% and 46%, respectively; hazard ratio with pMCS: 0.96; 95% confidence interval: 0.42 to 2.18; p = 0.92). At 6 months, mortality rates for both pMCS and IABP were 50% (hazard ratio: 1.04; 95% confidence interval: 0.47 to 2.32; p = 0.923).

CONCLUSIONS In this explorative randomized controlled trial involving mechanically ventilated patients with CS after AMI, routine treatment with pMCS was not associated with reduced 30-day mortality compared with IABP. (IMPRESS in Severe Shock; NTR3450) (J Am Coll Cardiol 2017;69:278–87) © 2017 by the American College of Cardiology Foundation.

Despite advances in treatment, mortality in acute myocardial infarction (AMI) complicated by cardiogenic shock (CS) remains high (1-4). Short-term mechanical circulatory support devices can be deployed to support the endangered circulation. Intra-aortic balloon counterpulsation (IABP) has been the most widely used mechanical circulatory support device for decades (5). A meta-analysis of smaller-sized studies and a large randomized controlled trial did not show a beneficial effect of IABP in the setting of CS after AMI (4,6,7). Today, IABP usage has a Class IIb recommendation in American guidelines and a Class III recommendation in European guidelines (8-11).

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The lack of efficacy of the IABP is likely to be, at least partly, the reason for the observed increased usage of more potent mechanical circulatory devices (5,12).

The percutaneous Impella platform (Abiomed, Danvers, Massachusetts) consists of the Impella 2.5 (maximum output 2.5 l/min) and Impella CP (maximum output around 3.7 l/min). It has been shown that Impella support in the acute situation is feasible and provides greater hemodynamic support when compared with IABP (13–16). However, neither of the 2 small randomized trials in patients with AMI had enough power to show differences in clinical outcomes, and 1 was prematurely stopped (15,16). The IMPRESS in Severe Shock (IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK) trial is an exploratory assessment of mortality and other safety outcomes comparing percutaneous mechanical circulatory support (pMCS) by the Impella CP with IABP in mechanically ventilated patients with CS in AMI.

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METHODS

STUDY DESIGN. The Academic Medical Center in Amsterdam designed and sponsored this multicenter, open-label, and randomized trial. Trial administration, data management, and statistical analysis were performed by the sponsor. The executive committee had unrestricted access to the data, and the authors analyzed the data and prepared the paper. The trial design was approved by the ethics committee at each participating center. The ethics committee waived the requirements for written informed consent before randomization to prevent treatment delay in patients who were in imminent danger of death. The requirement for obtaining informed consent to use the data varied depending on local ethical requirements. Informed consent was obtained from the legal representative without any undue delay. Alternatively, informed consent was obtained after recovery (and therefore, no informed consent was obtained in patients who died). An independent data and safety monitoring board and the ethics committees reviewed the interim results after each 10 included patients. During the inclusion period of the trial, the European Society of Cardiology guidelines for routine use of the IABP changed from Class II (may be considered) to Class III (not recommended) (10). The ethics committees were notified of this change and approved continuation of the trial. The study was conducted in accordance with the provisions of the Declaration of Helsinki as amended in Edinburgh, Scotland (17).

PATIENTS. Patients were eligible for the trial if they presented with an AMI with ST-segment elevation complicated by severe CS in the setting of immediate percutaneous coronary intervention (PCI). Severe CS was defined as a systolic blood pressure <90 mm Hg for longer than 30 min or the need for inotropes or vasopressors to maintain a systolic blood pressure >90 mm Hg. To select a patient population in even worse condition, patients only qualified if they were mechanically ventilated before randomization. Exclusion criteria were: severe aorto-iliac arterial disease impeding placement of either IABP or pMCS, known severe cardiac aortic valvular disease, serious known concomitant disease with a life expectancy of <1 year, known participation in this study or any other trial within the previous 30 days, or coronary artery bypass grafting within the preceding week.

TREATMENT. Eligible patients were assigned to treatment with pMCS by Impella CP with IABP (control group). Randomization was performed in a 1:1 ratio using an internet-based application. The moment of initiation of pMCS or IABP (before, during, or immediately after the PCI) was at the discretion of the treating physician. To achieve equal initiation of therapy for both groups, timing of randomization was equal to pMCS or IABP placement: immediately before, during, or after PCI.

All patients underwent primary PCI. In multivessel disease, the mode of revascularization (immediate or staged PCI of the nonculprit lesions) was left to the discretion of the operator. Duration of mechanical support was left to the discretion of the treating physician, and IABP or the pMCS device was extracted in accordance with daily clinical routine. Weaning was achieved by reduction of the trigger ratio (IABP) or amount of support (pMCS). Per protocol, crossover was not allowed; however, it did occur.

OUTCOMES. The primary study endpoint was 30-day all-cause mortality. The secondary endpoint was 6-month mortality. Descriptive endpoints included duration of mechanical ventilation; the need for and duration of inotropic and vasopressor therapy; renal replacement therapy; length of hospital stay; the amount of blood products needed; additional treatments, such as ICD placement and the need for surgical left ventricular assist device (LVAD) placement

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CS = cardiogenic shock

IABP = intra-aortic balloon pump

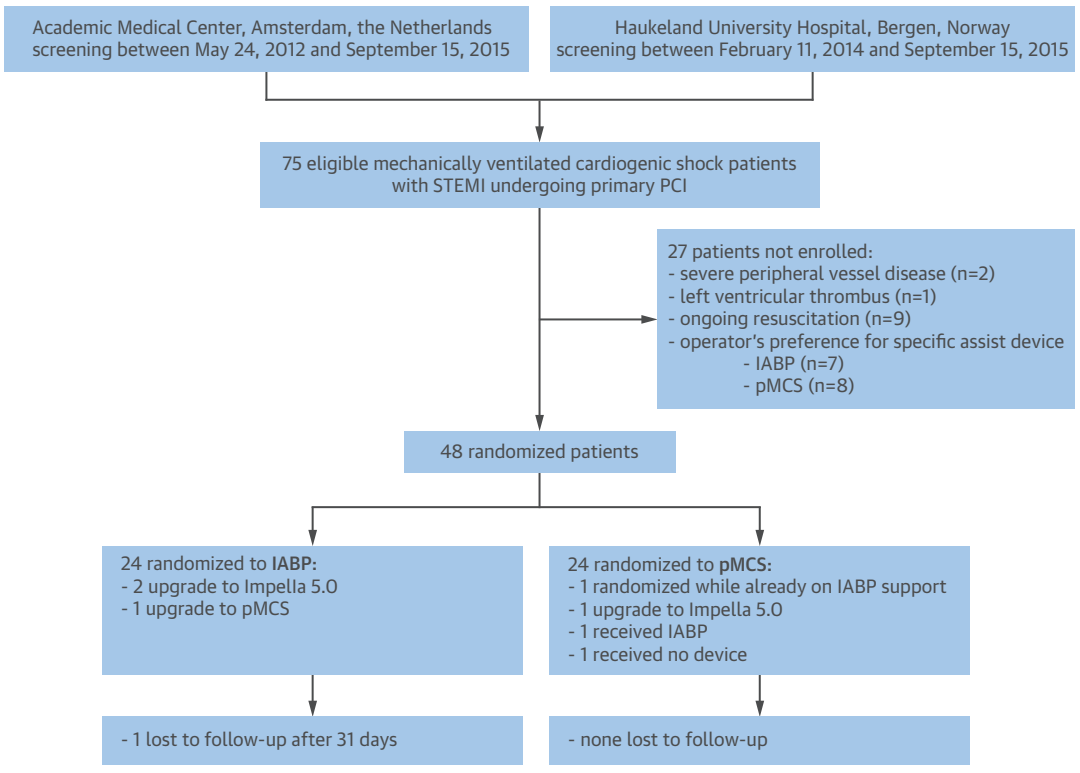
LVAD = left ventricular assist device

PCI = percutaneous cardiac intervention

pMCS = percutaneous mechanical circulatory support

ROSC = return of spontaneous circulation

FIGURE 1 Flow Diagram



Flow chart of the screening, randomization, and follow-up of the patients.

or heart transplantation; the occurrence of stroke, myocardial reinfarction, repeat PCI, coronary artery bypass grafting, major vascular complications, major bleeding, or hemolysis requiring extraction of the IABP or pMCS; device failure requiring extraction of the pMCS or IABP; and rehospitalization. Definitions can be found in the supplementary file. An independent clinical event committee adjudicated the events. Imaging parameters were assessed by independent local core laboratories that were blinded to the other trial data and randomization outcome (Online Appendix).

STATISTICAL ANALYSIS. On the basis of previous studies and our experience that survival is <10% in patients with severe shock, we assumed that treatment with pMCS would decrease the absolute 30-day mortality rate from 95% to 60%. On the basis of this assumption, a trial with 24 patients in each group would achieve 80% power, with a 2-sided alpha of 5%. The protocol allowed for a sample-size re-estimation after inclusion of 32 patients. At the interim analysis, mortality in the control group was much lower than anticipated, and there was no difference in mortality between the treatment groups. Therefore, adaptation of the sample size was not meaningful, and the Executive Committee decided to complete the study with 48 patients as an exploratory safety study.

All data were analyzed according to the intention-to-treat principle. In addition, a per-protocol analysis of the primary endpoint was performed. Cumulative mortality throughout the first 6 months following randomization was characterized with the use of Kaplan-Meier plots, with the log-rank test used for the comparison between the 2 groups. Descriptive endpoints and clinical course variables were not statistically tested because they are highly influenced by the number of deceased patients in both groups. Additional comparisons were made according to vital status at 30 days. Differences were assessed with the Fisher exact test or the chi-square test for binary endpoints and a Mann-Whitney *U* test for quantitative endpoints.

A post hoc subgroup analysis was performed in subgroups defined according to age (<75 or >75 years), sex, time to return of spontaneous circulation (ROSC)

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(>20 or <20 min), lactate level >7.5 or <7.5 mmol/l, TIMI (Thrombolysis In Myocardial Infarction) flow post-PCI, systolic blood pressure before IABP or pMCS placement (>80 or <80 mm Hg), and the presence or absence of traumatic injuries on admission.

RESULTS

PATIENTS. Between June 1, 2012, and September 15, 2015, a total of 48 patients were randomly assigned to either pMCS therapy (n = 24) or IABP (n = 24) (Figure 1). The baseline characteristics of the 2 groups were well balanced (Table 1). The mean age was 58 years, 79% were male, all patients were mechanically ventilated, 96% of the patients received catecholamines, and 92% had had a cardiac arrest before randomization.

TREATMENT. Randomization and placement of the pMCS or IABP took place after revascularization except for 8 patients in whom IABP or the pMCS was initiated before revascularization (3 in the IABP group and 5 in the pMCS group) (Table 2). The infarct-related artery was the left anterior descending (LAD) in the majority of the patients (65%) and 98% of the patients were treated with stent placement. The median duration of circulatory support was 48 h (IABP) and 49 h (pMCS). All patients were treated with catecholamines during admission to the intensive care unit, 31% received renal replacement therapy, and 75% were treated with therapeutic hypothermia (Table 3).

Of the patients in the IABP group, 1 patient subsequently received pMCS and was transferred to another hospital for treatment with extracorporeal life support oxygenation. Two patients received an alternative device, the Impella 5.0 (Abiomed, Aachen, Germany), after the IABP treatment, and 1 of them received subsequent extracorporeal life support and an LVAD at another hospital. Of the patients treated with the pMCS, 1 patient subsequently received the Impella 5.0. One patient was already on IABP support before randomization (inserted before the start of the primary PCI) and was randomized after the PCI to pMCS treatment. Formally, this patient constitutes a protocol violation, as IABP therapy before randomization was an exclusion criterion. One patient did not receive pMCS as the patient showed signs of recovery after randomization to receive device therapy.

OUTCOMES. At 30 days, mortality was similar in patients treated with IABP and pMCS therapy: 50% and 46%, respectively (hazard ratio [HR] with pMCS therapy: 0.96; 95% confidence interval [CI]: 0.42 to 2.18; p = 0.92) (Table 4, Central Illustration). At 6 months, the mortality rate was 50% in both groups (HR: 1.04; 95% CI: 0.47 to 2.32; p = 0.92). Only minor differences were found in an analysis restricted to the per-protocol population from which 3 patients treated with pMCS were excluded (Online Appendix). The Kaplan-Meier estimates for 6-month mortality in the per-protocol population were 52% in the IABP group and 48% in the pMCS group (HR with pMCS: 0.95; 95% CI: 0.41 to 2.21; p = 0.91).

The primary cause of death at 6 months was brain damage (46% of the deceased patients; 6 of 12 in the

TABLE 1 Baseline Characteristics

	pMCS (n = 24)	IABP (n = 24)
Age, yrs	58 ± 9	59 ± 11
Male	18/24 (75)	20/24 (83)
Body mass index, kg/m^2	25 (23–26)	26 (25–27)
Cardiovascular risk factors		
Current smoking	11/18 (61)	6/19 (32)
Hypertension	4/20 (20)	6/21 (29)
Hypercholesterolemia	4/20 (20)	5/21 (24)
Diabetes mellitus	2/22 (9)	3/23 (13)
Prior myocardial infarction	1/22 (5)	1/23 (4)
Prior stroke	0/22 (0)	1/23 (4)
Known peripheral arterial disease	2/23 (9)	0/23 (0)
Prior PCI or CABG	1/22 (5)	0/23 (0)
Hemodynamic variables before randomization		
Heart rate, beats/min	81 ± 21	83 ± 28
Mean arterial pressure, mm Hg	66 ± 15	66 ± 15
Systolic blood pressure, mm Hg	81 ± 17	84 ± 19
Diastolic blood pressure, mm Hg	58 ± 22	57 ± 13
Medical therapy before randomization		
Catecholamines or inotropes	24/24 (100)	22/24 (92)
Mechanical ventilation	24/24 (100)	24/24 (100)
Cardiac arrest before randomization	24/24 (100)	20/24 (83)
Witnessed arrest	22/24 (92)	17/20 (85)
First rhythm VT/VF	22/24 (92)	17/20 (85)
Time till return of spontaneous circulation, min	21 (15–46)	27 (15–52)
Traumatic injuries at admission	5/24 (21)	2/24 (8)
Blood values on admission*		
Lactate, mmol/l	7.5 ± 3.2	8.9 ± 6.6
Hemoglobin, mmol/l	8.6 ± 1.2	8.6 ± 1.2
Creatinine, mg/dl	96 ± 29	102 ± 22
Glucose, mmol/l	16.2 ± 4.7	14.1 ± 5.3
Arterial pH	7.14 ± 0.14	7.17 ± 0.17
Baseline echocardiography†		
Estimated left ventricular ejection fraction		
<20%	5/22 (23)	8/18 (44)
20%–40%	10/22 (46)	6/18 (33)
>40%	7/22 (32)	4/18 (22)

Values are mean ± SD, n/N (%), or median (25th to 75th percentile). *Values are present for the following number of patients: lactate (21 IABP and pMCS), hemoglobin (22 IABP and 21 pMCS), creatinine (23 IABP and 23 pMCS), glucose (23 IABP and 20 pMCS), and pH (16 IABP and 20 pMCS). †First echocardiogram made during admission during the first day. In 20 patients, the echocardiography was done before pMCS or IABP placement, and in 21 patients, after pMCS or IABP placement (within 24 h).

CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; PCI = percutaneous coronary intervention; pMCS = percutaneous mechanical circulatory support; VF = ventricular fibrillation; VT = ventricular tachycardia.

TABLE 2 Procedural Characteristics

	pMCS (n = 24)	IABP (n = 24)
Moment of device placement		
Device placement before revascularization	5/24 (21)	3/24 (13)
Device placement after revascularization	19/24 (80)	21/24 (88)
Infarct-related artery		
Left main	1/24 (4)	2/24 (8)
Left anterior descending	16/24 (67)	15/24 (63)
Left circumflex	6/24 (25)	3/24 (13)
Right coronary artery	1/24 (4)	4/24 (17)
Multivessel disease*	15/24 (63)	21/24 (88)
Immediate PCI of nonculprit lesion	3/15 (20)	4/21 (19)
Stent placement	23/24 (96)	24/24 (100)
Drug-eluting stent	22/23 (96)	22/24 (92)
Bare-metal stent	1/23 (4)	2/24 (8)
TIMI flow pre-PCI		
0 or 1	20/24 (83)	20/24 (83)
2 or 3	4/24 (17)	4/24 (17)
TIMI flow post-PCI		
0 or 1	1/24 (4)	0/24 (0)
2 or 3	23/24 (96)	24/24 (100)
SYNTAX score pre-PCI	23.2 ± 8.7	28.2 ± 10.6

Values are n/N (%) or mean ± SD. *>50% stenosis in nonculprit vessel.
TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

IABP group and 5 of 12 in the pMCS group). Death due to refractory CS occurred in 29% of the deceased patients (3 of 12 in the IABP vs. 4 of 12 in the pMCS therapy group).

In each group, 1 patient experienced an ischemic stroke during support. There was 1 major vascular complication in the pMCS group, a retroperitoneal bleeding after pMCS insertion (the patient had a calcified and stented vascular trajectory, but femoroiliac angiography seemed compatible with pMCS insertion, see Online Appendix for event specifications). There were more bleeding events during admission in the pMCS therapy group than in the IABP group (8 vs. 2, of which 3 and 1, respectively, were adjudicated as IABP or pMCS related). There were 2 patients in whom the presence of hemolysis influenced the decision to stop the pMCS support (in one patient, the pMCS support was stopped due to hemolysis in combination with an improved ejection fraction; and in the other patient, the pMCS was removed after the decision to withhold further therapy due to multiorgan failure, recurrent ventricular arrhythmia, hemolysis, and hemodynamic instability).

Follow-up echocardiography was performed and collected in all survivors except for 3 patients: 1 received a surgical LVAD, 1 was lost to follow-up after 31 days, and 1 was bedbound due to multiple sclerosis. Left ventricular ejection fraction after 2.5 months (median 191 days) was 46 ± 11% in the pMCS group and 49 ± 9% in the IABP group.

Subgroup analysis showed no significant interaction in 30-day mortality between the IABP and pMCS-treated patients with respect to age, sex, ROSC times, lactate levels on admission, moment of IABP or pMCS placement, systolic blood pressure before device placement, and traumatic injuries on admission (Online Appendix, Online Table 1).

When analyzing the combined study population, lower 30-day mortality rates were seen in patients who had ROSC in <20 min (19% vs. 70%; HR: 5.50; 95% CI: 1.82 to 16.58; p = 0.001) and patients with lactate level on admission lower than 7.5 mmol/l (29% vs. 60%; HR: 3.09; 95% CI: 1.09 to 8.74; p = 0.04) (Online Appendix, Online Table 2). A trend toward lower 30-day mortality was observed if therapy with pMCS or IABP was initiated before the primary PCI (25% vs. 53%; p = 0.16) and in patients who did not have traumatic injuries (44% vs. 71%; HR: 1.88; 95% CI: 0.70 to 5.07; p = 0.18) (Online Appendix). Trends in lactate and creatinine levels and inotrope and vasopressors usage can be seen in Online Figures 1 to 4. Also, characteristics of the survivors versus the nonsurvivors and more extensive cardiac function parameters are described in Online Tables 3 and 4.

DISCUSSION

This is the first randomized trial to compare Impella CP with the IABP in mechanically ventilated patients with CS complicating AMI. pMCS support was not associated with lower 30-day or 6-month mortality when compared with IABP support. Although this trial included only 48 patients, it is thus far the largest trial to randomly compare pMCS and IABP, and it is the only trial to use the Impella CP device.

To date, only a few randomized controlled trials have studied mechanical circulatory support in CS, highlighting the logistical and ethical challenges in conducting trials in these patients. In the setting of CS, 2 small trials have been performed with the Impella 2.5 pMCS, both using IABP therapy as the control therapy. The ISAR-SHOCK (Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock) trial randomized 26 patients between IABP and the Impella 2.5 in the setting of CS complicating AMI. The primary endpoint was the difference in cardiac index after 30 min of support, and the trial showed a higher cardiac index in patients treated with Impella than with IABP. Overall mortality was 46% in both groups (15). The IMPRESS in STEMI trial randomized between the IABP

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and Impella 2.5 in patients with cardiogenic preshock. This study was powered for a difference in left ventricular function. However, this trial was stopped prematurely due to a lack of enrollment after 21 patients had been enrolled (16).

In the present trial, we included mechanically ventilated patients with CS. Although the decision to start mechanical ventilation may be arbitrary and the moment of initiation may differ between physicians, it is a marker for worse clinical condition. We have chosen to use this criterion because it is easy to apply, is readily available, and does not require blood sample analysis or additional Swan-Ganz cardiac output measurements. Those inclusion criteria resulted in inclusion of patients with high lactate and low pH levels on admission, and all patients received catecholamines before randomization. Although we did not aim to include resuscitated patients, the inclusion criteria resulted in 92% of enrolled patients having a cardiac arrest prior to randomization. In addition, almost one-half (48%) of the patients had time to ROSC longer than 20 min. Traumatic injuries due to cardiac arrest were frequently present (15%). These criteria identified a unique patient population that is usually excluded from randomized CS clinical trials and resulted in a patient population with a high 30-day mortality rate of 48%. This is higher than in the most recently reported randomized trial on CS (IABP-SHOCK II [Intra-Aortic Balloon Counterpulsation in Acute Myocardial Infarction Complicated by Cardiogenic Shock] trial), which reports a mortality of 40% in patients randomized between IABP support and conventional therapy (n = 598) (4). Two previous studies compared IABP and TandemHeart (CardiacAssist Inc., Pittsburgh, Pennsylvania) in CS, with 30-day mortality rates of 44% (n = 41) (18) and 42% (n = 33) (19). Neither trial observed any difference in mortality between the patients treated with TandemHeart or IABP. A registry reporting on Impella 2.5 versus IABP in the setting of post-cardiac arrest shock reports mortality rates of 77% in patients treated with the device and 79% in patients treated with IABP (20). Two multicenter registries including patients with CS complicating AMI supported with a pMCS showed mortality at discharge of 49.3% (n = 154) and 30-day mortality of 64.2% (n = 120) (21,22).

A recent USpella registry analysis submitted to the U.S. Food and Drug Administration for the Impella pre-market approval for use in CS demonstrated a marked difference between patients who were likely to be included in randomized shock trials versus those who were not—the latter of whom resemble the population studied in the present trial (23). A considerable proportion of patients died due to anoxic brain damage (46%), compared with refractory CS or multiorgan failure (29%), or for other reasons (25%). This high rate of neurologically deceased patients is likely to be the result of the high percentage of resuscitated patients and longer times to ROSC. Nevertheless, our study resembles a real-life cohort in daily clinical practice of patients with CS complicating ST-segment elevation myocardial infarction.

In our study, bleeding occurred more often in the pMCS-treated patients than in the IABP-treated patients. During mechanical support, patients receive heparin in addition to standard dual antiplatelet therapy after PCI (aspirin and a $P2Y_{12}$ receptor blocker), which makes the occurrence of bleeding more likely, especially in patients with additional traumatic injuries on admission. Higher rates of

TABLE 3 Clinical Course During Admission

	pMCS (n = 24)	IABP (n = 24)
Mechanical circulatory support		
Duration of support (h)*	49 (28-76)	48 (24-77)
Crossover or upgrading to device with more support†	1/24 (4.2)	3/24 (12.5)
Other support before randomization‡	1/24 (4.2)	0/24 (0)
Mechanical ventilation		
Patients treated	24/24 (100)	24/24 (100)
Duration (days since device placement)	4 (3-9)	4 (3-10)
Catecholamines		
Patients treated	24/24 (100)	24/24 (100)
Duration (days)	3 (2-6)	3 (2-5)
Inotropic therapy (dobutamine)		
Patients treated	6/24 (25)	9/24 (38)
Duration (days)	0 (0-1)	0 (0-2)
Renal replacement therapy		
Patients treated	8/24 (33)	7/24 (29)
Duration (days)	17 (5-29)	7 (2-9)
Therapeutic hypothermia		
Patients treated	19/24 (79)	17/24 (71)
Premature ending of therapeutic hypothermia	3/19 (16)	1/17 (6)
Blood products during admission§		
Any blood products during admission	11/24 (46)	8/24 (33)
Packed red blood cells		
Patients treated	11/24 (46)	8/24 (33)
Number of units administered	6 (3-13)	3 (1-5)
Fresh frozen plasma	3/24 (13)	0/24 (0)
Platelets	4/24 (17)	1/24 (4)
Placement of implantable cardioverter-defibrillator	2/24 (8)	1/24 (4)
Length of stay (days)		
Intensive care unit	7 (3-16)	7 (4-10)
Hospital	16 (3-26)	10 (6-24)

Values are median (25th to 75th percentile) or n/N (%). *Sum of support duration of all given support devices, including upgrades. †One patient was upgraded from IABP to pMCS and transferred to another hospital to receive extracorporeal life support; 1 patient received pMCS and was upgraded to Impella 5.0; 1 patient was upgraded from IABP to Impella 5.0; and 1 patient was upgraded from IABP to Impella 5.0 and transferred to another hospital to receive extracorporeal life support and surgical LVAD. ‡One patient was already on IABP support before randomization and was randomized to pMCS support. §Only blood products in the hospital of randomization are taken into account.

LVAD = left ventricular assist device; other abbreviations as in Table 1.

TABLE 4 Clinical and Functional Outcomes

	pMCS (n = 24)	IABP (n = 24)	p Value	Hazard Ratio With pMCS (95% CI)
Mortality*				
30-day all-cause mortality	11 (46)	12 (50)	0.92	0.96 (0.42-2.18)
6-month all-cause mortality	12 (50)	12 (50)	0.92	1.04 (0.47-2.32)
Clinical outcomes at 6 months				
Cause of death				
Refractory cardiogenic shock	4 (17)	3 (13)		
Post-anoxic neurological death	5 (21)	6 (25)		
Other reason	3 (13)	3 (13)		
Stroke	1 (4)	1 (4)		
Hemorrhagic stroke	0 (0)	0 (0)		
Ischemic stroke	1 (4)	1 (4)		
Major vascular complication	1 (4)	0 (0)		
Major bleeding	8 (33)	2 (8)		
Device-related bleeding	3 (13)	1 (4)		
Retroperitoneal	1 (4)	0 (0)		
IABP/Impella puncture site	2 (8)	1 (4)		
Nondevice-related bleeding	5 (21)	1 (4)		
Gastro-intestinal bleeding	0 (0)	1 (4)		
Bleeding at other puncture site	1 (4)	0 (0)		
Other location	4 (17)	0 (0)		
Hemolysis requiring extraction of the device	2 (8)	0 (0)		
Device failure requiring extraction	0 (0)	0 (0)		
Surgical LVAD placement	0 (0)	1 (4)		
Heart transplantation	0 (0)	0 (0)		
Other surgery	2 (8)	0 (0)		
Myocardial (re)infarction	1 (4)	2 (8)		
Repeat PCI	0 (0)	3 (13)		
CABG	0 (0)	1 (4)		
Rehospitalization	5 (21)	1 (4)		
Cardiac	2 (8)	0 (0)		
Noncardiac	3 (13)	1 (4)		
Echocardiography at 6 months†				
Left ventricular dimensions and systolic function (n)	12	9‡		
Ejection fraction (%)	46 ± 11	49 ± 9		
End-diastolic volume (ml)	122 ± 41	120 ± 33		
End-systolic volume (ml)	65 ± 31	61 ± 21		

Values are frequencies (%) or mean ± SD, unless otherwise indicated. Additional information about events can be found in the Online Appendix. *Mortality is shown as Kaplan-Meier estimates. †First available echocardiogram after 2 months. Median follow-up time is 191 (176 to 297) days. ‡One patient with surgical LVAD, 1 patient lost to follow-up, and 1 patient bedridden due to multiple sclerosis.

CI = confidence interval; other abbreviations as in Tables 1 and 3.

bleeding in pMCS-treated patients compared with IABP-treated patients were also described in a registry comparing Impella 2.5 and IABP in a post-cardiac arrest population (n = 78), which found severe bleeding in 26% of the device patients versus 6% of IABP patients (20). Two large multicenter Impella 2.5 registries describe the rates of bleeding requiring transfusion of 24.2% and 17.5% and the rates of hemolysis as 7.5% and 10.3% (21,22). These complication rates are comparable to the pMCS in our study (33.3% bleeding and 8.3% hemolysis). The IABP-SHOCK II trial reports 20.7% bleeding in the IABP patients (and 20.8% in the control group). This is higher than the 8.2% bleeding in our IABP group.

Although discouraged, some crossovers and upgrades to other mechanical support therapy did take place: 3 in the IABP group and 1 in the pMCS group. Crossover or upgrading was solely at the discretion of the investigator. There was a trend toward more upgrading/crossover in the IABP group.

Upon initiation of our study, IABP therapy was still recommended in the guidelines for CS, but was downgraded to a Class III recommendation in the European guidelines and Class II in the American guidelines during the inclusion period of the study. After consultation with the institutional review board and in the light of the severity of clinical condition with higher mortality rates than in the IABP-SHOCK II study, the control therapy remained unchanged. In addition, after the interim analysis it was clear the study was underpowered to show a difference in mortality at 30 days, and the executive committee allowed it to proceed for exploratory purposes.

Although not adequately powered, our trial suggests that in patients with CS without selection on age, ROSC times, and pre-procedural traumatic injuries, no clear signal of superior outcome was observed in patients with pMCS support when compared with the IABP.

There may be several reasons why the pMCS-treated patients did not show improved mortality rates. A possible explanation is the unselective nature of the patients included in the study. In our study, 92% of patients had resuscitated cardiac arrest, which implies a prevalence of post-anoxic neurological damage present at the moment of randomization. Any kind of mechanical circulatory support may be of limited clinical utility in these patients. Another explanation might be that CS after AMI is not only a matter of low cardiac output. The shock syndrome also comprises an irreversible damage due to diminished organ perfusion and inflammatory responses. Hence, providing mechanical hemodynamic support may not be enough to reverse the damage that has already occurred. Although the Impella CP can provide up to 3.5 l/min of forward flow, it might still be insufficient to reverse severe CS with advanced end organ failure, especially as in clinical practice, long-term Impella CP support achieves <3.5 l/min hemodynamic support. In this trial, the main rationale for using Impella CP instead of a device that can provide even more hemodynamic support (e.g., Impella 5.0), was the need for a surgical cut-down for implantation. The Impella CP can be inserted percutaneously, which enables quick insertion even

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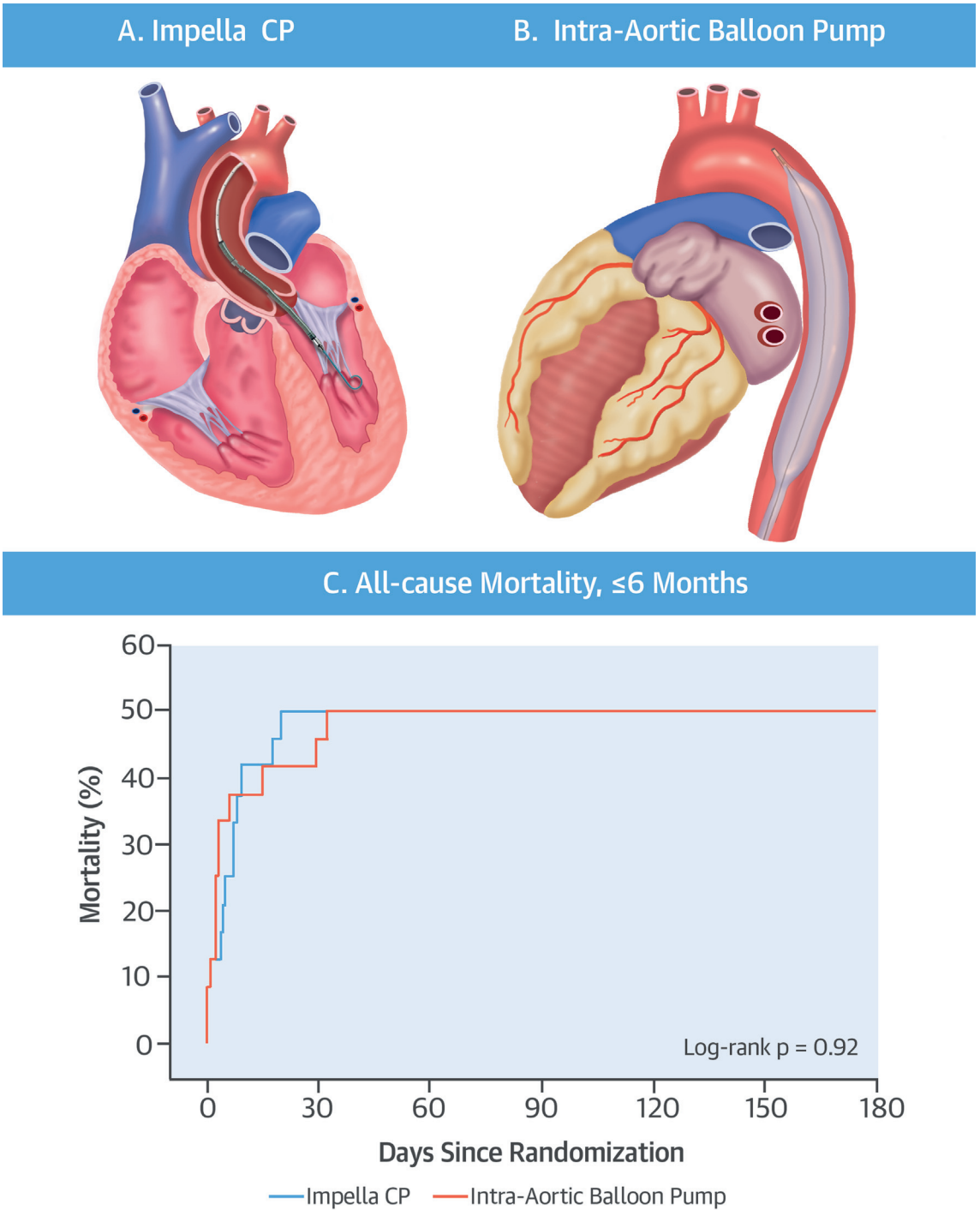
CENTRAL ILLUSTRATION **Impella CP Versus IABP in Cardiogenic Shock**



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(A and B) Schematic drawings of the heart and aorta showing the 2 mechanical support devices used in the study: **(A)** Impella CP (Abiomed, Danvers, Massachusetts); **(B)** the intra-aortic balloon pump (IABP). **(C)** Time-to-event Kaplan-Meier curves up to 6 months after randomization for all-cause mortality. LV = left ventricular.

before performing primary PCI. Earlier reports have demonstrated a better survival in patients who received a pMCS before primary PCI than in implantation post-PCI (22). Our data also shows a trend toward lower mortality rates in patients in whom either the device or IABP was initiated before the primary PCI (25.0% vs. 52.5% overall).

STUDY LIMITATIONS. A major limitation of this trial is its small number of patients. Adequately powered randomized clinical trials are needed to ascertain the value of pMCS in patients with CS after AMI.

CONCLUSIONS

In this explorative study, routine treatment with pMCS was not associated with lower 30-day mortality in patients with CS complicating AMI.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with AMI complicated by severe CS, treatment support with a pMCS device was associated with a 30-day survival rate similar to that achieved with IABP.

TRANSLATIONAL OUTLOOK: Further studies are needed to clarify the clinical characteristics of patients with CS who benefit from 1 mode of mechanical circulatory support more than another.

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KEY WORDS acute myocardial infarction, cardiogenic shock, intra-aortic balloon pump, mechanical circulatory support, randomized controlled trial

APPENDIX For the trial organization and supplemental methods as well as supplemental figures and tables, please see the online version of this article.